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Medical News Letter

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MEDICAL NEWS LETTER

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Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

Please forward changes of address for the News Letter to: Commanding Officer, U.S. Naval Medical School, National Naval Medical Center, Bethesda, Maryland 20014, giving full name, rank, corps, and old and new addresses.

FRONT COVER: Architectural Sketch of the new U.S. Naval Hospital, Long Beach, California. The 350-bed hospital was approved by contract on 16 March 1965. The work on pile foundations has been completed. The contract for building the superstructure was awarded on 18 Dec 1964 and work was started on 4 Jan 1965.

The hospital consists of 4 floors and a basement area. The basement area contains subsistence facilities which include dining rooms and galley. This basement, or lower ground floor area, contains an open court which permits both the officers and enlisted dining rooms to open out onto this planted area so that the basement aspect is not a confining aspect. Other elements in the ground floor basement space include pharmacy, navy exchange, staff lounge, medical storage, & mechanical services. The first floor of the hospital at ground level contains administration, clinics, and adjunct services. Also, the surgical suite is located at the heart of the ground floor area. Nursing units, 350 beds, are contained on the 2nd, 3rd, & 4th floors. The plan of the hospital is based on utilizing central services system. The hospital is equipped with automatic tray conveyor system extending from the central sterile supply in the basement up to the 4th floor nursing units. In conjunction with the hospital, a separate project for a 142-man barracks building is being constructed at the same time as the hospital.

The hospital site contains 30 acres and is located at the southwest corner of the intersection of Carson Street and the proposed San Gabriel River Freeway. The anticipated completion of the hospital is approximately 1 July 1966.

This hospital was sponsored by the Bureau of Medicine and Surgery in the FY 1963 Military Construction Program. The Military Construction Authorization Bill was ultimately cleared for the President's signature. On 25 Sep 1962 the Congress passed the Military Appropriation Act which included provision for construction of this hospital.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

FEATURE ARTICLE

PROLONGED MECHANICAL VENTILATION

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Extensive clinical experience has demonstrated the value of assisted or controlled mechanical ventilation for the management of patients with certain postsurgical, traumatic, and medical problems.[8] Artificial ventilation is now commonly used in the treatment of patients with inadequate respiratory function due to trauma, chest disease, chest surgery, pain, fatigue, certain types of poisoning, neuromuscular disorders, and iatrogenic causes. Military personnel would most likely become victims of trauma, poisoning by anticholinesterases, and acute respiratory failure due to neuromuscular disorders. Thus meticulous patient care, comprehension of certain mechanical principles, proper equipment and facilities are required in order to minimize morbidity and mortality associated with prolonged mechanical ventilation outside the operating room. Obviously, physicians involved in most disciplines of medical practice will encounter patients who require ventilatory management.

Accurate and rapid evaluation of the patient's signs, symptoms, and laboratory data are frequently necessary if respiratory therapy is to be initiated in time to be effective. While it is beyond the scope of this paper to describe in detail the evaluation of respiratory failure, examination should include patency of the upper airway, chest motion, chest auscultation, chest x-ray, vital capacity measurement with a Wright meter (or its equivalent), and arterial blood gas determinations (pH, pCO_2, and pO_2) in those patients whose respiratory function has not ceased or failed to a point that the necessity for airway maintenance and mechanical ventilation has become obvious. In many borderline cases ventilatory volume will meet the requirements for normal blood gas exchange but the reserve for additional ventilatory effort may be progressively diminishing; frequent examinations of the patient are required to avoid overlooking this type of impending respiratory failure. Complete confidence in nomograms for predicting ventilatory volumes in the absence of physical examination and arterial blood gas determinations is ill-advised.

When mechanical ventilation with equipment designed to apply pressure to the upper airway of a patient is being considered, an initial decision must be made regarding the method of airway management. The decision generally involves endotracheal intubation and/or tracheostomy. Endotracheal intubation usually via the nose, with or without the aid of topical anesthesia, is preferred in the adult patient in whom recovery is anticipated in 48 to 72 hours; beyond this time, tracheostomy is usually indicated. This general rule may be excepted in the infant who can be managed successfully for 2 to 3 weeks with the insertion of a Portex endotracheal tube which is properly attended. Under normal circumstances the tube used for the maintenance of an airway in an adult should be changed at least every 12 to 24 hours to avoid obstruction by crusted secretions. In the patient in whom tracheostomy is obviously required at the beginning of treatment, the procedure should be performed after the placement of an endotracheal tube so as to minimize the danger of tracheal obstruction due to compression, blood, or secretions.[5] Tracheostomy and endotracheal tubes should be used only with inflatable cuffs attached so that they can be inflated to the point that air will not escape during the positive pressure phase of respiration. Cuff inflation will minimize the hazard of aspiration of secretions or gastric contents. Over-inflation of the cuff may cause pressure necrosis of the tracheal mucous membrane especially in the membranous portion of the trachea, although this hazard is more commonly associated with motion of the tracheostomy tube or the introduction of bacterial infection secondary to improper tracheostomy care.

Once the indications for mechanical ventilation are identified and the airway has been established, a decision must be made as to the type of equipment to be used for prolonged treatment. There are two major methods of producing mechanical ventilation in a patient. One produces respiration by intermittently expanding the lungs with gas under positive pressure applied to the upper airway. In most instances a pressure of 10 to 20 cm of water is required for normal ventilatory volume. Obviously, wide variations in pressure requirements exist depending upon the patient's condition and disease process. However, normal respiratory function encompasses much more than maintenance of a fixed ventilatory volume. Humidification, efficient coughing, and deep breathing are important aspects of successful long-term management of ventilation.

In many instances ventilation is best achieved with a respirator setting which is at the lowest pressure, shortest inspiratory duration, and least expiratory resistance necessary to produce the desired volume of gas exchange for the patient. Normally, the duration of expiration or the pause for expiration should be longer than that of inspiration. A predetermined cycle of inspiration and expiration cannot be selected for patients in a routine fashion but must be evaluated with individual variations in the patients' respiratory functions. This is especially true in assisted respiration for patients who are dyspnic. Therefore, a respirator should be selected which is capable of variable inspiratory flow rates, variable durations of inspiration and expiration, and controlled humidification. It should have, also, a sensing device to trigger the machine in situations requiring assisted respiration and accurate control of delivered concentrations of oxygen.

Respirators available at the present time which apply positive pressure to the airway can be classified according to the cycling mechanism. Some ventilators are pressure cycled so inspiration ends when the pressure in the airway reaches a predetermined value. These ventilators are commonly known as pressure-constant volume-variable ventilators (Bennett PR–1 and PR–2, Bird Mark VII). Others are described as volume-constant pressure-variable ventilators in which inspiration ends at a pre-set volume (Air Shields, Bird Mark 17). The latter type are widely used on patients who require long-term ventilation because they tend to insure a fixed volume of gas delivery. Still other ventilators are time cycled and unrelated to pressure or volume of ventilation; inspiration ends at some pre-set time determined by the controls on the apparatus and is independent of the patient (Mörch). Most of the presently available equipment offer a combination of these cycling mechanisms. Recent improvements in ventilators include the addition of alarm systems (Air Shields), hot water humidification (Mörch), chest expansion sensing device (Bird), automatic intermittent deep breathing (Emerson), and ultrasonic nebulizers (Engström).

Humidification by bubbling oxygen through water at room temperature is not adequate for long-term ventilation. A heated nebulizer or vapor from hot water is required to increase the humidity to the level required in order to minimize airway obstruction due to crusted secretion. Monitoring the temperature of air delivered at the tracheostomy site is important in order to avoid burns or elevation of the patient's body temperature when heated humidification systems are used.

The other major method of artificial respiration involves the application of negative pressure to the entire body or at least to the thorax. This method most commonly utilizes a tank respirator (iron lung) or a cuirass respirator in which the thorax and/or abdomen are enclosed and exposed to cycling negative pressures. These ventilators can be used successfully if the patient is conscious and does not have a problem with his upper airway; however, they inhibit routine nursing care. Other ventilation methods of less importance include the rocking bed, phrenic nerve stimulation, and oxygen insufflation.

The primary hazards of mechanical ventilation involve trauma to the airway or lungs due to excessive motion of the connecting devices, over-inflation of cuffs attached to endotracheal or tracheostomy tubes, occurrence of atelectasis and/or infection, and excessive ventilatory pressures. The patient with normal cardiovascular function tolerates improper mechanical ventilation without difficulty; however, a patient who is not capable of compensation may experience harm, especially when mean airway pressure is elevated to a significant degree. This results in an increase in right auricular pressure and a decrease in the gradient between the auricular pressure and venous pressure in the peripheral veins. Thus, normal venous return is opposed, and cardiac output is adversely affected. Furthermore, a high airway pressure decreases pulmonary blood flow which in turn may result in elevated right ventricular pressure.[4] Thus intermittent positive pressure breathing may affect adversely the patient with perfusion problems. Uneven alveolar ventilation may occur in a patient with emphysema,

bronchiectasis, small airway obstruction, asthma, or chronic bronchitis. These and other conditions tend to magnify the undesirable effects of positive and, especially, negative pressure ventilation on the circulatory system.[2]

Another possible hazard is oxygen toxicity with resultant lung damage secondary to inadvertent administration of oxygen in high concentrations. Recent evidence indicates oxygen-powered ventilators utilizing air dilution venturi valves will deliver high concentrations of oxygen when nebulizers are activated or when high airway pressures are required to produce adequate ventilatory volume. Inadvertent administration of 70 to 90 per cent oxygen may occur,[3] and pulmonary damage may result after 4 to 5 days exposure to this concentration of oxygen.[7] Delivered gas oxygen concentration should be monitored to avoid this hazard and to identify changes in ventilation/perfusion ratios.

Once long-term mechanical ventilation is undertaken a concomitant arrangement should be made for intermittent deep breathing. This can be accomplished with the use of an Ambu bag. Newer types of ventilating equipment have this capability built into the respiratory cycle. Intermittent positive pressure with bronchodilators may prove a useful adjunct. Chest physical therapy and proper positioning of the patient are frequently valuable in mobilizing retained secretions by vibration and percussion of the chest, postural drainage, deep breathing, and manual assistance to coughing.[1,6] Proper tracheal suctioning technique utilizing sterile catheters and sterile irrigating solutions is extremely important. The hazards of introducing infection under the circumstances of improper tracheal technique are significant and may prove fatal. Bronchoscopy is seldom necessary with the proper regime of associated therapy but should not be neglected when indicated.

Under ordinary circumstances long-term mechanical ventilation should not be attempted in a hospital unless intensive care or respiratory unit facilities are available. Beecher, et al., clearly indicate the advisability of such units when they observe that treatment of the majority of critically ill patients crosses the borders of many specialties of medicine and team work is required for optimal care.[1] Such facilities require skilled nursing personnel, frequent observations of the patient by physicians, and appropriate laboratory and monitoring equipment.

The primary goal of mechanical ventilation is the maintenance of gas exchange during critical periods of respiratory failure. Equipment must be selected and adjusted so as to eliminate hypoxia, facilitate removal of carbon dioxide and maintain adequate humidification in the air passages. Normally, equipment which produces respiration by intermittently expanding the lungs with gas applied under positive pressure to the upper airway through an endotracheal tube or tracheostomy is most effective. In most instances volume-constant ventilation combined with intermittent deep breathing, simulated coughing, chest physical therapy, and proper tracheal suction techniques will decrease the hazards of long-term mechanical ventilation of patients.

Artificial ventilation is best handled in hospitals with proper intensive care or respiratory unit facilities, trained nursing personnel, laboratory facilities with equipment for determination of blood pH, pCO_2, and pO_2, and physicians who understand the ventilatory equipment and are available for frequent observations and examinations of the patient. When these criteria are met, the mortality and morbidity associated with mechanical ventilation can be minimized.

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MEDICAL ARTICLES

SEVENTEEN YEAR SURVIVAL AFTER REMOVAL OF RECURRENT GASTRIC CARCINOMA

William Y. Inouye MD and William H. Erb MD, Philadelphia, Penna. From The American Journal of Surgery 109(5): 656-659, May 1965.*

The prognosis of patients with gastric carcinoma in whom tumor transplants subsequently develop in the line of the incision has been extremely bad (1-7). Indeed, a recent compilation of all patients surviving gastrectomy for carcinoma of the stomach by fifteen years listed only fifty-three cases. We thought it of interest, therefore, to report on a patient who recently died at the Philadelphia General Hospital at the age of seventy-two years, which was seventeen years after excision of such an implant that appeared three months after the original gastric resection for carcinoma

Case Report

The seventy-two year old white man (case no. 24-21-25) was readmitted to Philadelphia General Hospital on April 12, 1963 with a presumptive diagnosis of recurrent gastric carcinoma. On November 19, 1945 he had undergone subtotal gastrectomy for adenocarcinoma of the stomach with no evidence of metastasis. The pathologic report was as follows: "The specimen consists of distal half of stomach measuring 12.5 cm along the lesser curvature and 24 cm along the greater curvature. Six centimeters proximal to pylorus on lesser curvature, there is a fungating ulcerated lesion 7 cm in diameter, the wall of the stomach at the edge of the lesion being 4 cm in thickness. The greater omentum is attached to the greater curvature. A few enlarged lymph nodes contained therein were free of tumor."

He did well until three months later at which time a 3.5 by 3 by 1 cm lesion was found in the abdominal incision, and this was resected to the fascia. The pathologic report was as follows: "Specimen consists of an elliptical section of skin and subcutaneous tissue and fat measuring 2 by 4 by 6 cm. Imbedded in this is a rubbery-feeling tumor mass about 1 by 3 by 3.5 cm. It feels adherent to the under surface of the dermis. The skin and subcutaneous tissue appear normal in color. The tumor mass cannot be separated from the skin, appearing to have no capsule. The cut surface is greyish yellow, is very soft and almost necrotic in the center and cuts with increased resistance. Diagnosis: adenocarcinoma, metastasis showing essentially the same features as those of the primary gastric tumor."

In the interim between 1946 and 1963, he had done well, and weight had been maintained at 165 pounds. Two months prior to the third admission, epigastric pain developed which radiated through to the back about one hour after meals. There was no history of vomiting, dysphagia, anorexia, or melena. An upper gastrointestinal series revealed the presence of another gastric lesion. On abdominal examination a large transverse scar was present which was free of any recurrent tumor. The liver, kidney, and spleen were not palpably enlarged, and no intra-abdominal masses were felt. Rectal examination revealed brown feces.

Laboratory studies included: hemoglobin value, 13.2 gm per cent; white blood cell count, 6,900 per cu mm; bromsulphalein, no retention. The gastric analysis showed no free acid and a maximum of 87 clinical units total acidity. The cytologic study of the gastric washing was reported as class 3 (doubtful). On gastroscopy a polypoid tumor measuring 2 cm in diameter was seen in the midportion of the gastric pouch.

At operation on April 23, 1963 a firm tumor was found within the gastric pouch; the tumor did not involve the gastrojejunostomy anastomosis, and the surgeon thought that it could have been either a second primary or a recurrent tumor. The liver was not grossly involved with tumor, and no enlarged

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TABLE I

GASTRIC CANCER RECURRENCE IN WOUNDS

Year	Author	Interval between Gastrectomy and Wound Recurrence (mo.)*	Survival after Wound Recurrence Noted (mo.)	Miscellaneous
1955	Ackerman	12.0	96.0	Died of lymphosarcoma; no evidence of recurrent carcinoma of stomach
1957	Meadows	2.5	7.5	
1957	Bush	3.0	8.0	
1958	Cronin	7.17	Still alive 18 months later	Axillary metastasis removed 21 mo. after gastrectomy
1960	Fortner and Lawrence	2.5	15.0	
		3.0	28.0	
		3.8	2.0	
		4.0	4.0	
		5.0	2.0	
		11.0	3.0	
		22.0	0.75	
		24.0	17.0	
		38.0	6.0	
1961	Sonneland	19.0	Still alive 18 months later	Hepatic metastasis noted 37 mo. after gastrectomy
1963	Inouye and Erb	3.0	206.0	

* Average interval was 10.7 months.

lymph nodes were noted. A 95 per cent subtotal gastrectomy, splenectomy, and retrocolic gastrojejunostomy were carried out. The pathologic report was adenocarcinoma of the stomach.

On the fifth postoperative day after a sudden episode of cyanosis, tachypnea and hypotension, the patient died. Postmortem examination was denied.

Comments

In 1928 cancer of the stomach was reported to be inoperable in 75 per cent of patients, and only three instances of five year survival could be located in the current literature by one author [8]. Although there has been an increase in the rate of operability to 91 per cent, resectability to 74 per cent, and possible curability to 55 per cent [9], carcinoma of the stomach remains a diagnostic and therapeutic challenge to the modern practitioner. The five year survival rate was only 7.17 per cent in a group of 12,728 patients reviewed by Lipp and Phillips in 1960 [10]. Iatrogenic implantation of gastric carcinoma in the abdominal wound is a serious complication which further minimizes chances for long time survival. Wound recurrence represents a technical error which unfortunately is associated with removal of many types of tumor [1-4]. Its incidence has been reported to be 1.5 per cent in patients subjected to curative gastrectomy [1]. Recurrence of tumor at the primary site, however, may be a manifestation of its spread prior to surgical implantation or a technical error. In a series of autopsy cases of patients who underwent gastrectomy for carcinoma of the stomach, only four of ninety-two patients were free of recurrence [11].

The interval between gastrectomy for carcinoma and wound recurrence averaged 10.7 months for fifteen patients reported on by various authors [1-7]. (Table 1.) Eleven of these patients were dead between three weeks and twenty-eight months after recurrence was noted in the scar. Two were still alive at eighteen months, but both had evidence of other metastases. Another patient was apparently well at forty-eight months, but he subsequently died of lymphosarcoma eight years after the operation for recurrent cancer of the stomach. There was no evidence of cancer of the stomach at death; apparently excision of the implant was successful [12]. Although our patient died after repeated gastric resection, he survived seventeen years after surgical extirpation of wound recurrence. Therefore, we believe that although the majority of these patients die very shortly after metastases are apparent, there is an occasional patient in whom skin recurrence is the sole manifestation and its excision may lead to long term survival. In view of the fact that this is a minor procedure solitary skin recurrences should be promptly excised in the absence of other recurrences.

Certain surgical principles have been previously emphasized in an attempt to minimize this problem. These include excisional biopsy whenever possible: "en bloc" excision, gentle handling of the tumor, placement of covers on serosal surfaces to prevent glove and instrument contamination, changing of gloves and instruments, placement of ligatures proximal and distal to the point of resection, and application of antitumorigenic agents within the bowel lumen, or irrigation of wound at the time of closure [2, 5, 13, 14]. The use of antitumorigenic drugs is not without danger; irrigation of tumor-contaminated wounds by use of chemotherapeutic agents has been reported to result in a higher recurrence rate than in control animals having saline irrigation of wounds [14, 15]. In man a higher incidence of wound dehiscence has been noted with use of nitrogen mustard [16].

Survival for fifteen or more years after gastrectomy for carcinoma of the stomach was not reported until 1954 by Anglem [17] and Pack [18]. An additional fifty cases have been recorded [9, 18, 19-30]. The incidence of patients surviving more than fifteen years after gastrectomy for adenocarcinoma of the stomach at the Philadelphia General Hospital between 1934 and 1948 was six patients in 670, or 0.9 per cent. Two of these six patients died seventeen years after surgery, one is the subject of this paper and the other died an unrelated traumatic death; a third patient died at home twenty-four years postgastrectomy. Three patients are still alive fifteen, fifteen, and nineteen years after gastric resection. This compares with 0.47 per cent reported by Ransom [21] and 0.32 per cent reported by Shahon et al.[22]. Factors bearing on the survival of any given patient are thought to be a slow growing tumor [31], duration of symptoms [19, 27], "biological predeterminism" [32], penetration of serosa by the tumor, presence or absence of distant metastasis, type of tumor [33, 34], and sinus histiocytosis of regional lymph nodes [20]. Age and sex of the patient surviving gastrectomy appear to have little if any bearing on the survival rate [20, 29]. Among nineteen patients surviving over five years after gastrectomy for carcinoma of the stomach at the Philadelphia General Hospital (1934 to 1958), the average age was sixty-one years (range: forty-five to eighty-two years); there were eleven male and eight female patients.

Treatment should be surgical extirpation of the tumor-bearing scar with an adequate margin of normal appearing tissue. The treatment for recurrent intra-abdominal lesions must be guided by the gross findings at reoperation. When lymph nodes were free of tumor at the time of both operations, ten year survivals have been reported after the second procedure [25]. In agreement with Cronin [3] an "optimistic surgical attitude" is advocated toward the management of recurrent carcinoma.

Summary

Recurrence of carcinoma of the stomach in the surgical scar is discussed and vigorous surgical treatment is advocated when no other recurrences are suspected. A patient surviving seventeen years after removal of skin recurrence of gastric carcinoma is reported on.

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EFFECT OF FASTING OR A KETOGENIC DIET ON GROSS BODY COMPOSITION IN OBESITY*

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Although prolonged fasting for weight reduction in obesity has been extensively evaluated and found to produce consistent, adequate weight loss, few studies have focused on the changes in gross body composition that must accompany such periods of starvation. It has been reported that large deficits in body potassium result from fasting, and it is also known that adipose tissue contains negligible concentrations of potassium, the major portion of this cation residing in muscle or lean tissue. However, correlation of the known potassium deficit to lean tissue loss has not been made, even though quantitation of the extent of lean tissue loss would seem of prime importance in assessing the clinical value of fasting for weight reduction. Thus, in an attempt to determine such correlations, gross body composition and metabolic balance studies were made on a group of obese males and as a standard of reference, the alterations noted after fasting were compared to a similar period on a low calorie, high fat, or ketogenic diet. The ketogenic diet was chosen because it has been reported to produce greater weight loss than an isocaloric balanced diet, and also because the metabolic changes attending it resemble fasting.

The patient group comprised seven males with obesity, but without other overt disease. The mean weight of the group was 115.6 Kg and this weight was estimated to be 44% due to adipose tissue. The study was conducted on a metabolic ward and the study period for each patient was 24 days, divided into 10 days of fasting, 4 days of a 1000 calorie mixed diet to allow a return towards equilibrium, and 10 days of the ketogenic diet. This diet was calculated at 1000 calories, which was composed of 82% fat, 14% protein and 4% carbohydrates, and analysis showed it contained 7.3 gm/day of nitrogen, 56.5 mEq/day of potassium and 283.5 mEq/day of sodium. Routine balance techniques were employed and the excreta analyzed for nitrogen, potassium and sodium. The total body potassium content was determined by counting the naturally occurring isotope, potassium-40, in a whole body scintillation spectrometer. From this information, plus body weight, gross body composition was derived, using reported constants. Body fat is taken as the difference between the measured total weight and the derived lean body weight. This two-compartmental method of estimating body composition is analogous in principle to measuring lean body weight by total body water methods.

Results

The patients tolerated both study periods equally well and during both had metabolic acidosis with ketonemia and ketonuria. The balance data for the entire group (table 1) showed that there was a mean weight loss of 9.6 Kg/period while fasting compared to 6.6 Kg/period on the diet. Similarly, the nitrogen loss of fasting was almost twice that of the diet. In contrast, potassium and sodium balances were both markedly negative while fasting but positive on the ketogenic diet.

Table 1

Balance Data (10 day periods)

Balance	Fast Period	Ketogenic Period
Nitrogen (gm/day)	−12.6	− 7.0
Potassium (mEq/day)	−43.4	+ 2.5
Sodium (mEq/day)	−63.0	+85.7
Weight (Kg/day)	− 0.96	− 0.66

The mean loss in total body potassium of the group due to fasting was 15.1 gm or 385 mEq, and this contrasted sharply with a loss of only 0.6 gm during the ketogenic period.

The mean changes in gross body composition for the group revealed that the mean 9.6 Kg total weight

* Presented at the Golden Anniversary Session of the American College of Physicians, March 22, 1965, at Chicago, Illinois.

loss of fasting was due to a 6.2 Kg fall in lean weight and only 3.4 Kg loss in body fat. In contrast, during the ketogenic diet period, a 6.4 Kg loss of body fat occurred in the group with only a 0.2 Kg fall in lean weight. Expressed in a different manner, the weight reduction of fasting was 65% due to a lean tissue loss and only 35% to a decrease in adipose tissue, while the weight change with the ketogenic diet was only 3% due to lean tissue loss and the mean total amount of body fat lost was twice as large as that of the fast period. Further calculations showed that although there was an 8% overall loss of weight with fasting, the per cent body fat at the end of the period actually increased from 44 to 45%. This increase in relative per cent body fat can be accounted for by the fact that the greatest amount of weight loss was due to lean tissue reduction. These changes are summarized in Table 2.

Table 2

Summary of Body Composition Changes Noted

	Fast		Ketogenic	
Weight	Kg	%	Kg	%
Total Body	−9.6	–	—6.4	–
Lean Body	−6.2	65	−0.2	3
Body Fat	−3.4	35	−6.2	97

The ideal weight reducing program for obesity should produce significant weight loss without catabolism of lean tissue. Or conversely, adipose tissue mobilization and removal should occur without change in the lean body tissue. Although low calorie, balanced diets produce this result, the weight reduction is not generally rapid and because of the low rate of weight loss, patients and their physicians often despair of any meaningful results. Because of the marked weight reduction that occurs with fasting, in association with the mild anorexia and euphoria that develop, this therapeutic program has received a high degree of clinical acceptance by obese patients. However, the data presented in this study suggest that the weight reduction during ten days of total caloric deprivation is indiscriminately contributed to by lean tissue catabolism as well as fat. Fasting beyond ten days may produce decreasing rates of lean tissue breakdown, since it has been shown by Drenick and his colleagues that the daily rate of total body potassium loss slackens as the fast period extends beyond 30 days. However, in fasts up to 102 days they noted that the percentage loss of the original body potassium content always exceeded the percentage loss of original body weight and at 102 days, the body potassium loss was as great as 35% of the original content. The physiologic wisdom of incurring such wastes in lean body tissue is questionable.

The low-calorie, high fat diet used in this study produced consistent, striking weight loss without apparent catabolism of lean tissue and was well accepted by the patients. This aspect of the study supports the contention of Kekwick and Pawan and others, that low calorie, ketogenic diets are especially effective in treating obesity. The reasons such a diet gives better results than other dietary compositions is imperfectly understood. Recently these workers have shown in animals that with a low calorie, high carbohydrate diet, extremely efficient and increased utilization of the diet occurs, whereas with an equi-calorie, high fat diet, decreased utilization of the dietary energy resulted with a consequent greater weight loss. In any event, the ketogenic diet resembles fasting in terms of the ketosis, acidosis and mild anorexia that ensue and this may be an added factor in influencing caloric restriction by the patient.

In conclusion, data has been presented which compared the gross body composition in seven obese males after equal periods of fasting and of a low-calorie, high fat diet. The results show that the weight lost while fasting was 65% due to lean tissue and only 35% to adipose tissue decrease. In contrast, the weight change while on the high fat diet was only 3% due to lean tissue loss and the mean total amount of body fat lost exceeded that of fasting. These results suggests that although clinically desirable weight reduction occurs during fasting, it is at the expense of lean tissue, which is physiologically undesirable.

FROM THE NOTE BOOK

CHEMOTHERAPY OF DRUG-RESISTANT TUBERCULOSIS

The increase of drug-resistant tuberculosis has given impetus to the search for new anti-tuberculosis drugs. The drugs so far available have in general been disappointing because of weak antibacillary activity or high toxicity. The major drugs, isoniazid, streptomycin, and PAS, remain therefore the drugs of choice for previously untreated tuberculosis, the new minor drugs being reserved as the second line of attack for patients whose treatment with the major drugs has failed because of drug resistance.

Minor Anti-Tuberculosis Drugs

The minor drugs now used in clinical practice are ethionamide, pyrazinamide, cycloserine, viomycin, kanamycin, and thiacetazone. New drugs, at present under investigation include capreomycin, ethambutol, and 4, 4-diisoamyloxythiocarbanilide ("isoxyl"; thiocarlide).

Ethionamide.—Ethionamide is a derivative of isonicotinic acid. It is a powerful drug whose anti-tuberculosis activity *in vitro* lies between those of isoniazid and streptomycin. There is no cross-resistance with any drugs except thiacetazone and substituted thioureas. Acquired resistance to ethionamide usually involves cross-resistance with thiacetazone, and acquired resistance to thiacetazone often involves cross-resistance to ethionamide. However, natural resistance to thiacetazone in anonymous mycobacteria or in few "wild" strains of *Myco. tuberculosis* does not usually involve ethionamide. The optimum dose is 20 mg. per kg. body weight (about 1 g. daily in man). Unfortunately this dose often gives rise to nausea, vomiting, and other gastrointestinal symptoms. Ethionamide, 1 g. daily, given with pyrazinamide or cycloserine to British patients caused gastrointestinal upsets sufficiently severe to cause treatment to be stopped in 22% of 117 patients, and 0.5 g. of ethionamide daily given with the same drugs caused treatment to be stopped in 9% of 42 patients. Yet among 67 Chinese patients given 0.5 g. of ethionamide daily with isoniazid only 2% stopped treatment because of gastrointestinal intolerance. Variations in the frequency with which patients tolerate ethionamide may be attributed to differences in the determination of the patient to continue treatment, the intensity of the persuasion and encouragement to which the patient is subjected, the nature of the companion drug, and racial factors. The administration of ethionamide in enteric-coated tablets or per rectum is unsuitable because of irregular absorption, but it is better tolerated if given as a single dose last thing at night, combined if necessary with a sedative. The N-propyl derivative appears to cause much less gastrointestinal upset and is now under clinical trial in Britain. Liver damage and mental disturbance are rare but serious complications of ethionamide treatment.

Pyrazinamide. Pyrazinamide is a pyridine derivative. It is a highly effective anti-tuberculosis drug and has no cross-resistance with other drugs. Unfortunately it is toxic to the liver, and because of this the dose in man should not be greater than 40 mg per kg. This dose of pyrazinamide combined with ethionamide and cycloserine produced an elevation of serum transaminase activity in 8% of 117 British patients. Estimation of serum transaminase levels every 2 weeks during treatment gives early indication of liver damage, usually before jaundice appears, and liver function usually returns to normal soon after pyrazinamide has been withdrawn. Used in this way under close medical observation pyrazinamide has proved to be a safe drug. Other tests of liver function are of little value for giving early warning of liver damage due to pyrazinamide. In a trial in Madras pyrazinamide, 30 to 40 mg per kg was given to 46 malnourished patients and no clinical evidence of liver damage was observed during a year of treatment; however, no transaminase estimations were made. Pyrazinamide causes an increase in the blood uric acid content which may give rise to gout, but the symptoms respond to aspirin or salicylate.

Cycloserine. Cycloserine is derived from *Streptomyces orchidaceus* and is of low tuberculostatic activity. No cross-resistance with other drugs has been reported. It is a toxic drug causing psychotic symptoms, depression sometimes leading to suicide, and convulsions. Even with small doses of 0.5 to 1 g daily serious toxic effects have been reported in 7% of patients. Cycloserine should be given only under close medical supervision.

Viomycin. Viomycin is derived from *Streptomyces puniceus* and has a weak anti-tuberculosis activity. Acquired viomycin resistance is associated with kanamycin resistance, but the reverse is not true (one-way cross-resistance). Viomycin resistance is usually associated with capreomycin resistance. Viomycin causes vestibular damage and deafness and also renal damage and electrolyte disturbances. The dose is 4 or 5 g weekly.

Kanamycin. Kanamycin is derived from the neomycin series of antibiotics obtained from *Streptomyces fradiae* and is a weak anti-tuberculosis drug. Acquired kanamycin resistance is usually associated with capreomycin resistance but not with viomycin resistance. The toxic effects are like those of streptomycin, but kanamycin is much more likely to produce irreversible deafness. Deafness has been reported in 2 of 53 patients given 1 g 3 times weekly, in 2 of 64 patients given 2 g twice weekly and 7 of 60 patients given 10 mg per kg 5 times weekly.

Thiacetazone. Thiacetazone is a thiosemicarbazone. Acquired thiacetazone resistance is usually associated with ethionamide resistance and vice versa. It has little place in the treatment of drug-resistant tuberculosis because of its cross-resistance with ethionamide. Ethionamide is a much more powerful drug than thiacetazone and should therefore be given in preference to thiacetazone. Where ethionamide treatment fails because of the emergence of ethionamide-resistant organisms subsequent treatment with thiacetazone is not likely to succeed because these organisms are likely also to be resistant to thiacetazone. Thiacetazone has been shown to be an effective companion drug for isoniazid in the treatment of newly diagnosed patients with drug-sensitive organisms. Because of its cheapness and low toxicity it may replace PAS as the companion drug for isoniazid in the developing countries.

Capreomycin. Capreomycin is obtained from *Streptomyces capreolus.* Acquired viomycin or kanamycin resistance is usually associated with capreomycin resistance. The toxicity and therapeutic potency of capreomycin are being investigated. Its toxic effects appear to be similar to those of streptomycin. Preliminary reports of its use in pulmonary tuberculosis are encouraging.

Ethambutol. Ethambutol is a synthetic compound. No cross-resistance has been observed. Diminution in visual acuity has been reported in about 10% of patients receiving 25 to 50 mg per kg daily. The ocular toxicity appears to be reversible when the drug is withdrawn. Its use in drug-resistant tuberculosis is under assessment.

4, 4-Diisoamyloxythiocarbanilide ("isoxyl"). This drug is a thiourea derivative and no toxicity has been reported in man. Its value in drug-resistant tuberculosis is unknown. In Hong Kong new cases of pulmonary tuberculosis in which the organisms were reported to be sensitive to isoxyl and isoniazid before treatment with these drugs had a much lower bacteriological conversion rate than a control group given PAS and isoniazid. In this investigation a high incidence of pre-treatment isoxyl resistance was reported.—Abstract from Abstracts of World Medicine 38(1): 7–8, July 1965.

NINTH ANNUAL SEMINAR ON PROPHYLAXIS AGAINST STREPTOCOCCAL INFECTIONS

The Ninth Annual Seminar on the Prophylaxis Against Streptococcal Infections sponsored by the Armed Forces Epidemiological Board will be held at U.S. Naval Training Center, San Diego, California, on Monday and Tuesday, 27 and 28 September 1965.

Activities desiring to send representatives to this seminar should submit letter requests to BUMED, Attention Code 316, in accordance with BUMED Instruction 1520. 8A as soon as possible.

NEWS ITEM

Recently, Saul Robinson MD, pediatric cardiologist from San Francisco, Calif., visited the U.S. Naval Hospital, Yokosuka during his trip to Japan to attend the Fifth Far East Session of the American College of Physicians. Doctor Robinson gave an address, "Congenital Pediatric Cardiac Problems," to the entire staff. Following a hospital staff luncheon, Doctor Robinson conducted a pediatric cardiology clinic. Doctor Robinson served as a special consultant to the Surgeon General, USAF, for the American College of Physicians meeting. He is also the pediatric cardiology consultant to commanding officers, U.S. Naval Hospital, Oakland, and Letterman General Hospital.—Submitted by CAPT R. E. Faucett MC USN, Chief of Medicine, USNH, Yokosuka, Japan.

SMALL-INTESTINE ULCERATION AND ENTERIC-COATED POTASSIUM CHLORIDE

There have been many warnings that enteric-coated potassium chloride preparations as well as enteric-coated combinations of thiazide diuretics and

potassium chloride cause small-intestinc ulceration, oftcn with obstructivc symptoms, and occasionally with perforation. Nevertheless, the promotion of enteric-coatcd potassium preparations continues.

Clinical Studies. Two pharmaceutical companies, Ciba and Merck, conductcd a survey of 488 hospitals in several countries (F. D. Lawrason ct al., JAMA 191:641, Fcb 22, 1965) in search of patients with constricting ulcers of the small intestinc. Of the 395 such patients discovered, only about half could be shown, on reviow of their charts, to have receivcd potassum chloride or potassium chloridc-diurctic therapy. Thc authors concluded: "There appears to be an increasc in the numbcr of ulcers of the small intcstine bcing reported, whether or not associated with spccific medication. Nevertheless, the incidcnce must be exccedingly low considering the millions of patients taking diuretics and potassium." Other cvidence makes these findings questionable.

Studies of patients with small-bowel ulceration have bcen carricd out in Swedcn and in various cities in the United States, including Brooklyn, Los Angeles, Minneapolis, Baltimore, Norfolk, and Daytona Bcach, with a total of 129 cases reported to the Small Bowel Ulcer Rcgistry (Jewish Hospital, Brooklyn). Of 125 patients in whom a detailed drug history was obtained, ingestion of potassium chloride in coated form was definitely established in 93 per ccnt and was probablc in another three per cent. Most patients ranged in age from 40 to 70 years and suffered from hypertensive or other cardiovascular disease. Obstruction occurred in 107 of thc 125 patients, perforation in 20 and bleeding in four patients. In some patients, morc than one complication was noted. Intestinal ulceration contributed to or was directly responsible for the deaths of several patients. All of the investigators in this study believe that a localized, circumferential ulcer of the small bowel, as distinguishcd from other types of ulceration, is a specific lesion almost always associated with the use of coated potassium preparations.

Two investigators have reported an incidence of ulceration of the small intestine as high as two to three per cent in outpatients given coated thiazide-potassium chloride preparations for the treatment of hypertension or congestive heart failure (D. R. Baker et al., JAMA 190:586, 1964; M. W. Donner et al., Maryland State Med J). Outpatients from the same clinics treated with non-enteric-coated thiazide diuretics alone havc failed to yield a single casc of small-intenstine ulceration.

Animal Studies. Experimental studies in dogs (S. J. Bolcy, ct al., JAMA 192:763, May 31, 1965) and monkcys (F. D. Lawrason et al., cited above) havc shown no ulcerations of the small intestine with non-coated thiazidcs alonc, but ulcerations wcre produced with coatcd tablcts of thiazides in combination with potassium chloridc (Esidrix-K—Ciba; Anhydron-K—Lilly; Anhydron-KR—Lilly; HydroDiuril-Ka—Mcrck; Hydropres-Ka—Merck; Naturctin c K—Squibb) or coated potassium chloride alone. Thc ulcerations appcarcd to rcsult from vcnous stasis attributable to absorption of high concentrations of potassium chloride by thc vcins of a short segment of small bowel.

Potassium Supplementation. The need for supplementary potassium and thc mcans by which it is administered must be carefully analyzed for each patient receiving potassium-wasting diuretics. In the absence of congestivc heart failure and digitalis therapy, hypertensive patients do not routinely require additional potassium when treated with Thiazide diuretics. However, such patients should be told to rcport symptoms of unusual muscle weakncss or fatigue, and should have periodic chccks of serum potassium. A diet containing foods rich in potassium usually suffices to correct any deficit. If additional supplemental potassium is rcquired, 10% to 20% solutions of potassium chloride can be used. (See The Medical Lcttcr 7:26, 1965, for a discussion of food sources and supplements of potassium chloride). The nausca and vomiting sometimes occurring with potassium chloride preparations is minimized if the medication is taken immediately aftcr mcals or with a full glass of water. Liquid potassium preparations containing other anions than the chloride are likely to be less effective in restoring normal acid-base balance.

Potassium chloride should not be regarded as a drug that can be administered without hazard as a supplement to diuretic therapy. Potassium chloride preparations should be given only when there is a specific indication for their use, and when dietary measures are inadequate. If supplcmentation is necessary, liquid preparations should be used. When employed in the coated form, either alone or in combination with coated thiazide preparations, potassium chloride presents a serious and unnecessary risk.—The Medical Letter 7(15): 57-58, July 16, 1965.

LUNG CANCER

The incidence of lung cancer has greatly increased in the past 50 years. Long-term survival data is poor. Evidence now suggests that bronchogenic carcinoma may be a long time evolving and that significant extension or widespread metastases may be present by the time the patient develops the first symptom. The routine chest film is an unsatisfactory method of uncovering truly early lung cancer, and we may have to await the development of a better diagnostic test if real inroads are to be made into this calamity. On the other hand, at least in part, the epidemic nature of this disorder may be prevented by elimination of atmospheric pollution, especially the personal one represented in the present-day cigarette.

Many systemic signs occur in relation to lung cancer that appear to be mediated or influenced by something that the tumor makes or possesses. These systemic manifestations may sometimes precede symptoms relative to the tumor and divert the clinician's attention from the thorax or other primary sites. Once recognized for what they are, these manifestations may prompt a search for the silent underlying malignancy. Furthermore, it is possible that these manifestations may act to hasten demise, and the patient may be significantly benefited if these abnormalities can be eliminated or improved. —Abstract from Disease-a-month, Carcinoma of the Lung, Including Systemic Manifestations by Melvin J. Krant, Thomas C. Chalmers, July 1965.

HEART VALVE TRANSPLANTS

London. A team of surgeons from Guy's Hospital reported in a recent issue of Lancet their results of 12 heart valve transplants taken from donors who had died from causes other than heart disease. The follow-up period of recipients of the homologous aortic valves varied from 12 to 31 months. Results have been excellent in three cases, good in six and fair in three. Artificial heart valves have been used with good results for some time. Some specialists, however, would prefer to use a substitute that approximates the original tissue as closely as possible. Problems of rejection are not as overwhelming in homologous heart valve transplants as commonly feared, according to the London group. —Abstract from International Medical News, pg. 21, August 1965.

THE ETIOLOGY OF CONTINUING MEDICAL EDUCATION IN THE UNITED STATES

The year 1965 marks the two hundredth anniversary of the founding of a School of Medicine at the College of Philadelphia (University of Pennsylvania) the first school of medicine in the English Colonies of North America. Prior to 1765, young men entered the medical profession after having served three or more years of apprenticeship to a practising physician. This custom, nevertheless, prevailed long after the founding of medical schools.

Doctor John Morgan of Philadelphia was one of relatively few Colonial physicians who were fortunate enough to supplement their preceptorial training by going to Europe for formal medical instruction leading to the doctorate in medicine. At this time young practitioners who could afford it were inclined, like Morgan, to go to the University of Edinburgh which stressed anatomy and bedside instruction.

When Dr. Morgan returned from Edinburgh in 1765 he was invited to give the commencement address at the College of Philadelphia whose trustees had already agreed to establish a medical school. His address, published as A Discourse Upon the Institution of Medical Schools in America was the primer of American Medical Education. It can still be read with profit by medical educators. —Abstract from Medical Arts & Sciences X1X(2): 49, Second Quarter, 1965.

NAVAL MEDICAL RESEARCH REPORTS

U. S. Naval Dental School, NNMC, Bethesda, Md.

1. Dental Caries and Nutrition in South Vietnam: MR 005.02–0001.09 Report No. 4, Jan-Feb 1965.

U. S. Naval Medical Research Institute, NNMC, Bethesda, Md.

1. Phosphorescence of Calcified Tissues: MR 005. 12–5000.02 Report No. 10, 1964.
2. Transillumination as a Means of Studying the Fundus of Small Animals: MR 005.13–1500.06 Report No. 2, April 1964.
3. A Monogenetic and Seven Digenetic Trematodes of Amphibians and Reptiles From Palawan Island, Philippines: MR 005.09–1606.01 Report No. 16, July 1964.
4. The Lung Worm Angiostrongylus Cantonensis of Rodents on Tiawan (Formosa) and the Offshore Islands: MR 005.09–1606.01 Report No. 15, September 1964.
5. Presidential Address: MR 005.02–0011.01 Report No. 5.
6. A Review of Current Concepts and Practices Used to Control Body Heat Loss During Water Immersion: MR 005.13–4001.06 Report No. 3.

7. Characteristics of Insoluble Protein of Tooth and Bone I. Flourescence of Some Acidic Hydrolytic Fragments: MR 005.12–5000.02 Report No. 11.
8. Anapbylactoid Reaction of the Mouse to Dextran: MR 005.01–0021.01 Report No. 5.
9. Ophthalmoscopy of Pigeons Using Transillumination: MR 005.13–1500.06 Report No. 1.
10. On the Assimilation of Energy from Inorganic Sources in Autotrophic Forms of Life: MR 005.03–0301.09 Report No. 2.
11. Reduction and Re-oxidation of the Disulphide Bonds of Soy Bean Trypsin Inhibitor: MR 005.06–0001.01 Report No. 24.
12. Importance of Preventing Renal Vascular Collapse During Period of Renal Ischemia in Kidney Transplantation: MR 005.02–0020.01 Report No. 4.
13. A Review of Current Concepts and Practices Used to Control Body Heat Loss During Water Immersion: MR 005.13–4001.06 Report No. 3.

U. S. Naval Medical Research Unit No. 3, Cairo, Egypt

1. The Fleas (Siphonaptera) of Egypt. Host-Parasite Relationships of Cricetid Rodents (Family Cricetidae, Subfamily Gerbillinae)[1]. MR 005.09–1402.3.
2. Ergebnisse der zoologischen Nubien-Expedition 1962: MR 005.09–1402.5.
3. A case of Brucella Spondylitis, January 1965.

U. S. Naval Medical Field Research Laboratory, Camp Lejeune, N. C.

1. Effect of pH on Human *Mycroplasma* Strains: MR 005.09–1501.1.6, March 1965.
2. Relationship of Rhinovirus Infection to Mild Upper Respiratory Disease: MR 005.09–1204. 4.15, April 1965.
3. Patterns of Adenovirus Infections in Marine Corps Personnel: MR 005.09–1204.4.16, April 1965.
4. Physical Training in Confined Spaces. I. Evaluation of the Universal Gym-A Preliminary Report: Task MR 005.01–0030.5.1, May 1965.
5. The Role of Mycoplasma (Pleuropneumonia-Like Organisms) in Human Disease: MR 005.09–1501.1.7, June 1965.
6. Test of Shelters, Extendible, Medium: MF 022.03.04–8006, July 1965.

U. S. Naval Submarine Medical Center, Submarine Base, Groton, Conn.

1. Effects of Acute Hypoxia and Hypercapnia on Pulmonary Circulation: MR 005.14–3002–4.13 Report No. 426, July 1964.
2. Color Mixture Functions at Low Luminance Levels: MR 005.14–1001–1.38, October 1964.
3. Conservative, Non-Surgical Management of Appendicitis: MR 005.14–3002–4.19, November 1964.
4. New Developments in High Pressure Living: MR 005.14–3100–3.04, November 1964.
5. Copying Noisy Radio Code Messages: MR 005.14–1001–2.17, December 1964.
6. Studies of Ciliary Mucus Transport in a Closed Cabin Atmosphere: MR 005.14–3002–4.18 Report No. 443, December 1964.
7. Differential Color Sensitivity in the Purple Region: MR 005.14–1001–1.39, January 1965.

DENTAL SECTION

NAVAL DENTAL RESEARCH REPORTS

The Naval Dental Corps can well take pride in its participation in the 43rd General Meeting of the International Association for Dental Research (IADR). Fifteen reports from the Naval Dental Corps' intramural research program were presented. This balanced program is broadly diversified, ranging from basic science through tissue response to clinical procedures, to efficient dental operatory design.

The intramural program's general task is to conduct research toward improved methods for the diagnosis, treatment, and prevention of oral disease in Naval and Marine Corps environments. Its objectives are: (1) to develop dental health programs for specific operational requirements ashore and afloat, (2) to provide support to the overall patient-care program and (3), to conduct the necessary basic research in support of operational and applied problems.

Only those intramural research projects which had reached the definitive data stage were reported at the IADR. Many readers will find some abstracts more interesting than others; however, the full group will be presented, to acquaint the reader with the scope of the Navy's intramural research program. In forthcoming issues, it is planned to reproduce the abstracts of two Navy IADR reports in each issue of the *U. S. Navy Medical News Letter*. After these IADR abstracts have been completed, it is planned to present abstracts of the remaining projects of the current intramural dental research program.

These IADR abstracts are reproduced with the permission of the Editor, Journal of Dental Research.

CAPT K. C. Hoerman, DC USN, is principal investigator on two research projects: Metabolic Activity of the Salivary Gland, and Qualitative and Quantitative Evaluation of the Organic Components in the Normal and Abnormal Human Tooth. Having previously served at the Dental Research Facility, Great Lakes, Illinois, and at the Naval Medical Research Unit #3, Cairo, UAR, CAPT Hoerman is presently Head, Chemistry Division, Dental Research Department, Naval Medical Research Institute, Bethesda, Maryland. A. Y. Balekjian, B. S. (Chemistry), and S. A. Mancewicz, B.S., M.S. (Chemistry), are American Dental Association Research Associates at NMRI. A guest scientist at NMRI from 1958 to 1965, Miss Mancewicz was recently transferred to the ADA Headquarters research program in Chicago, Illinois.

CDR W. R. Shiller, DC USN is currently principal investigator on two research projects: Oral Health in the Antarctic, and Effects of Stresses of Submarine Life of Oral Health. Having previously served a tour of duty at the Dental Research Facility, Great Lakes, Illinois, followed by a tour in USS JASON, AR–8, CDR Shiller reported for duty at the U.S. Naval Submarine Medical Center, U.S. Naval Submarine Base New London, Groton, Connecticut, in January 1964.

THE KINETICS OF THE AFTERGLOW PROCESS OF CALCIFIED TISSUES AT 89° KELVIN

Proceedings, 43rd General Meeting, IADR, 22-25 July 1965. A. Y. Balekjian, K. C. Hoerman and S. A. Mancewicz, Naval Medical Research Institute, Bethesda, Md.

The decay rate constants for the afterglow process in human enamel, dentin and bone at liquid N_2 temperatures revealed apparent conformational differences between the two types of tissues. These data were obtained on a filter phosphorimeter at approximate excitation and emission spectral maxima. Appropriate modifications have been made on a monochromated (diffraction grating) instrument so that the kinetics of phosphorescence may be studied under more idealized conditions. The decay rate constants and half-life time were calculated on the basis of an exponential decay process of c–at type. For all the calcified tissues the process was found to be di-phasic in nature with the initial decay being fast followed by a slower decay having half lifes in the range of 3 to 4 seconds. These kinetic data were compared to those obtained with globular proteins such as human serum albumin and soybean trypsin inhibitor. It was noted that enamel displayed decay rate constants and half-lifes more consistent with the globular proteins.

PERIODONTAL HEALTH OF SUBMARINE SCHOOL CANDIDATES: A CORRELATIVE ANALYSIS

Proceedings, 43rd General Meeting, IADR, 22-25 July 1965, William R. Shiller, Submarine Medical Center, USN Submarine Base New London, Groton, Conn.

An effort is being made to describe the parameters of periodontal health of naval personnel selected for submarine service and to evaluate factors related to periodontal health in these men.

The periodontal conditions of the selectees are evaluated using the periodontal index of Russell, the debris and calculus scores are assigned by the technique of Greene and Vermillion, a dental questionnaire is administered to discover dental habits, and psychological evaluations are accomplished by using standardized personality and motivation tests. These tests are the Personality Inventory Barometer (PIB) and the Self-Reported Motivational Questionnaire (SMQ).

Analysis of 95 Enlisted selectees for submarine training revealed a mean periodontal index of .13, a mean debris score of 1.387, and a mean oral hygiene index of 1.893. Correlative analyses revealed a significant positive relationship between the debris score and the periodontal index; a negative relationship between the frequency of toothbrushing and the periodontal index. A negative relationship was found between anxiety test indicators and the frequency of toothbrushing.

It is concluded that the level of periodontal health is comparatively high in submarine school candidates, that individual hygiene is closely related to

good periodontal health and that the psychological tests used revealed only a few relationships between personality and periodontal health factors.

ULTRASONICS AND PERIODONTAL THERAPY—A REVIEW OF CLINICAL AND BIOLOGIC EFFECTS

Green, G. H. Sanderson, A.D., Jour Periodont 36(3):232–238, May-June 1965.

Ultrasonic dental equipment was first used for cavity preparation, and the earliest published reports of its use for that purpose contained conflicting evidence concerning the clinical and biological effects. Later, an increasing number of generally favorable reports on the use of ultrasonic equipment for periodontal therapy began to appear. The use of an ultrasonic dental unit was especially advocated for oral prophylaxis. However, probably because of the earlier reports, questions about the safety of periodontal applications of utrasonic energy still persist. The purpose of this review of the literature, therefore, is to provide an evaluation of the clinical and biological effects on the tissues produced by the use of ultrasonic dental equipment for periodontal therapy.

Ultrasonic energy has been utilized as a medical therapeutic agent for more than thirty years, and it has repeatedly been stressed that its injudicious use can result in severe, irreversible damage to many tissues of the body. It has been correctly pointed out, however, that the effects of ultrasonic therapy as applied in medical practice cannot be strictly related to the effects of ultrasonics as used in dental practice, since the energy output of medical equipment, which vibrates from 800 to 4,000 kilocycles per second, is so much greater than the energy output of dental equipment, which only vibrates from 25 to 29 kilocycles per second.

The portable unit now in use is designed primarily for scaling procedures but can be adapted for other procedures such as curettage. It has a vibration frequency of about 25 kilocycles per second at an amplitude of .0015 cm. depending on the size and shape of the tip. The tip action is neither radiant nor electrical; it is mechanical in action. This unit converts an electrical frequency of 60 cycles per second to a vibrating frequency of between 23 and 26 kilocycles per second.

When the histologic effects of ultrasonic and manual curettage were compared, the ultrasonic technique and manual curettage were found to be equally effective.

Stanley prepared an excellent review of the literature on the high-speed effects and ultrasonic dental instrumentation on oral tissues, and concluded that these techniques are biologically acceptable when adequate precautions are observed by the operator.

In 1955, Zinner introduced ultrasonics into the field of periodontics. He removed calculus deposits from teeth with an ultrasonic tip and water coolant, and reported very little bleeding and no adverse subjective clinical symptoms.

In 1957, two different teams of investigators reported their comparisons of special ultrasonic tips, devised for scaling teeth, with conventional hand scalers. The study of in vivo applications of ultrasonic scalers showed that only light pressure was necessary for calculus removal. Patients preferred the Cavitron; cementum was virtually unharmed by a flat, unsharpened working point; and comparatively little hemorrhage was associated with the ultrasonic scaling procedure. The in vitro study reported that cavitation of a fluid coolant, with no positive pressure applied, produced debridement of root surfaces. Mechanical fragmentation and dislodgment of calculus were also observed. Under magnification, hand-scaled root surfaces showed fine lines and scratches, while surfaces scaled with Cavitron tips had a rippled, satin-like appearance.

Although no significant biological changes in humans, monkeys, or dogs have been reported when dental ultrasonic techniques were applied in the manner currently in clinical use, numerous investigators have demonstrated that severe, irreversible tissue damage can occur if considerable care and skill are not exercised. However, the same findings are also applicable to the use of the more conventional rotary dental instruments. The application of a constant hard pressure, for instance, will result in tissue damage whether the application is by means of the ultrasonic instrument or of low-speed rotary instruments. Tissue damage will also occur with either ultrasonic or high-speed rotary instruments if a water coolant is not properly used. Therefore, it can be assumed that any damage resulting from ultrasonic procedures is caused by the effects of frictional and absorbed heat and not by any unidentified type of energy produced by ultrasound.

The predominant evidence indicates that well-trained and carefully supervised dental assistants, as well as properly trained dentists, can safely use the dental ultrasonic unit for rapid removal of supragingival calculus. The unit can remove gross deposits of calculus more quickly and efficiently than can

hand scalers and should therefore prove to be an excellent addition to the periodontist's armamentarium.

(Abstracted by: CAPT P. C. Alexander, DC USN, U. S. Naval Dental Clinic, Long Beach, California.)

LEGAL RESPONSIBILITY OF THE DENTIST

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The dentist is legally required to possess and exercise the skill and care that the reasonably prudent dentist in the locale would possess and exercise under similar circumstances. When the dentist does not provide this standard of care, he becomes legally liable to the patient for any injuries that may result.

The law acknowledges that bad results may occur even when the dentist abides by the standard. The dentist is not legally liable for bad results if he has abided by the standards of care.

With some exceptions, the patient also must show that the injury was caused by the failure of the dentist to conform to the standard of care.

The dentist should not "guarantee" the results of dental treatment. Once he makes a guarantee, the law imposes on him a legal test much more severe than the standard of care.

The dentist should not perform service without the consent of the patient. He should inform the patient of the dental conditions present, recommend a course of action, then ask the patient whether he wants the dentist to proceed.

When a dentist breaks off a needle tip or a root tip, leaving the fragment embedded in the patient's jaw, he is liable for malpractice damages if he does not inform the patient of the mishap and if he does not try to remove the tip.

The dentist is required to take a case history before administering an anesthetic and to use only standard or accepted anesthetics, drugs and technics.

Once dental treatment has been started, the dentist has a legal duty not to abandon the patient.

The dentist is the owner of roentgenograms and, because they are one of his best weapons in defense of a malpractice lawsuit, he should not release them to a patient.

In the absence of fraud, the dentist is entitled to any fee to which the patient may agree in advance of treatment.

The dentist is legally liable for the negligent acts of his assistants and hygienists in the dental office.

The dentist is advised to have ample malpractice insurance from the first day to the last day of his practice. When a dentist is threatened with a malpractice claim, he should contact his insurance company immediately. He should not attempt to handle the matter himself and he should not contact the patient, meet with the patient's attorney, or answer the attorney's letters.

PERSONNEL AND PROFESSIONAL NOTES

Change of Command—U.S. Naval Dental School. CAPT Kenneth Lee Urban, DC USN, relieved CAPT Arthur R. Frechette, DC USN, as Commanding Officer of the U.S. Naval Dental School, National Naval Medical Center, Bethesda, Maryland, on July 30, 1965, in a traditional Navy change of command ceremony. During the exercises, RADM F. M. Kyes, DC USN, Assistant Chief of the Bureau of Medicine and Surgery (Dentistry), and Chief of the Dental Division, presented, on behalf of the President of the United States and the Secretary of the Navy, the Legion of Merit to CAPT Frechette. "For exceptionally meritorious conduct in the performance of outstanding service from October 1956 to May 1965 as Head of the Professional Branch and Deputy Chief of the Dental Division, Bureau of Medicine and Surgery, and as Commanding Officer of the U.S. Naval Dental School," CAPT Frechette was cited for extraordinary professional ability and resourcefulness. He retired as of August first to assume new responsibilities as Executive Secretary of the International Association for Dental Research.

CAPT Urban served as Head of the Enlisted Education Department in 1955 and as Head of the Officer Education Department from 1956 to 1959 during a previous tour of duty at the Naval Dental School.

Born in Perryville, Missouri, CAPT Urban is a dentist's son and has four brothers, all of whom entered the professions of dentistry or medicine. He was graduate from St. Louis University School of Dentistry in 1937 and joined the Navy the same year. In 1960 he won his Master's Degree in Education at American University, Washington, D.C.

CAPT Urban's work in the field of dental education began in 1947, when he assisted in planning the

organization and curriculums still used for Naval Dental Technicians Schools, after which he established and directed the Dental Technicians School at the U.S. Naval Training Center, San Diego, California.

In 1950 he went to Guam as officer in charge of the School for Dental Practitioners, where natives of Samoa and the Caroline Islands learned to be dental practitioners in the Trust Territories. Next, from 1952 to 1955, he was assigned to the Naval Dental Technicians Schools at Great Lakes, Illinois, in charge of a unified service program in which some 500 enlisted Navy and Air Force students were trained in the duties of general and prosthetic dental technicians.

CAPT Urban has served as executive officer at the U.S. Naval Dental Clinic, Washington, D.C., from 1959 to 1961; at the U.S. Naval Support Activity in Naples, Italy, and on the staff of the Commander, Fleet Air Mediterranean; and for the past year as commanding officer of the U.S. Naval Dental Clinic, Washington, D.C., and staff dental officer, Naval District, Washington.

Pilot Study on Dental Abstract Journal. The National Library of Medicine has entered into a cooperative arrangement with the American Dental Association, the PHS Division of Dental Public Health and resources, and the National Institute of Dental Research to conduct a pilot study leading toward an abstract journal for the world's dental literature. The project seeks to provide the first comprehensive coverage of international research literature related to dentistry and oral health.

"There is presently no comprehensive abstract service covering the world's scientific literature in oral health, dental science and practice." Dr. Luther L. Terry, Surgeon General of the Public Health Service said. "In this effort, several elements of the Public Health Service are working cooperatively with a U.S. professional scientific organization to improve basic scientific communications. This represents an interesting cooperative effort which may well serve as a model for similar activities in other subject matter fields."

The American Dental Association will receive and review abstracts of articles from the world's major dental journals and from selected non-dental journals, research will be covered, with specific subject areas to include oral biology, chemistry, physiology, and nutrition; cause and occurrence of dental disorders; dental materials and technology; dental health communications and information; and social and behavioral research related to dentistry. Ultimately some 250 dental journals, as well as a large number of non-dental publications, would be covered in the abstract journal. Publication of approximately 9,000 abstracts annually is proposed. Approximately half of the abstracts will be obtained from established sources in the United States. The remainder will be prepared by the faculty of the Hadassah School of Dentistry of Hebrew University, Jerusalem, under the direction of Dr. Ino Sciaky, dean of the school. NLM is supporting the preparation of abstracts in Israel under its special foreign currency program under a government contract with Israel's Program for Scientific Translations.

The decision to establish a journal of abstracts will be made in August 1965, on the basis of experience gained in the trial period.

Policy on Training Dental Enlisted Personnel. Formal schools are maintained to provide basic, specialized, or advanced technical knowledge and skills. However, it is not presumed that such courses will completely meet Navy requirements at all levels. For this reason, *inservice training,* as an extension of school training, is essential as a function of all commands.

Class "A" and "C" schools provide fundamental training to enlisted personnel so they may be productive as they continue their training in the field. Some subjects, such as typing, are not included in the basic school curriculum because the skill is not immediately required. Such skills can be developed on an individual basis by the command.

Enlisted personnel are trained continuously *to increase their value to the Navy.* Preparation for advancement in rating is properly an individual responsibility. The command responsibility is to direct the efforts and provide assistance when and where needed. Individuals who are able to progress with a minimum of assistance should be encouraged to do so, regardless of rate or rating. Those who require assistance should receive organized instruction for the required subjects. A highly efficient method to determine the areas where assistance is needed is to administer a challenging examination for each subject area.

The Manual of Qualifications for Advancement in Rating, NAVPERS 18068A, indicates the *minimum* requirements of knowledge and skills for Dental Technicians at each level. It is the basic source for development of school curricula and inservice training subject matter. Inservice training

manuals for Dental Technicians are presently in the process of complete revision. As soon as they are available, they will automatically be distributed to ships and stations having dental personnel.

In the interim, subject matter should be revised locally to conform with the requirements indicated in the "QUALS. MANUAL" at each rate or rating level.

OCCUPATIONAL MEDICINE SECTION

LEADERSHIP IN THE CONTROL OF ENVIRONMENTAL HAZARDS

WHAT ARE THE ENVIRONMENTAL PROBLEMS TODAY?

Thomas S. Ely, M.D., Rochester, New York, Proceedings of the President's Conference on Occupational Safety, Washington, D.C. 23–25 June 1964, Bulletin 263, pages 129–134.

The Conference is on occupational safety. The workshop is concerned with the environmental aspect of this topic. This paper is about present problems. So, I will be outlining some of the current environmental hazards of workers. "Environment" must be interpreted broadly here, and include not only chemical and radiation aspects, but also such factors as mechanical, thermal, and bacterial.

First, let us consider deaths as a kind of ultimate injury. Of almost 2 million deaths last year (1,800,000), an estimated 101,000, or about 1 in 20, were accidental. Almost half of these accidental deaths were workers. However, of the 45,900 worker deaths, less than one-third were work deaths—those of direct concern here. This is an estimated 14,200 deaths, and although this represents only one-seventh of all accidental deaths, it is still 14,200 too many.

It is estimated that less than 10 percent of work deaths were due to occupational "disease," and more than 90 percent were due to occupational "injury". These words take on different meanings at different times, but here "injury" means that the death followed the casual accident by a short time, and "disease" means that the death was a relatively long time later. Thus, death due to mechanical violence, drowning, or electrocution is called "injury", and death due to lead poisoning or silicosis is called "disease."

It is interesting to note that a worker is twice as likely to die accidentally off the job as on, and even when figured on the basis of time, if one assumes that not many die accidentally while asleep, the average worker was safer on the job. In the safer occupational groups, such as trade and manufacturing, this difference is striking. When the factory worker comes through the gate in the morning and begins his work at a large machine he is entering a safer environment than the one he left, from the standpoint of survival. I suspect this is because he left the most dangerous machine parked outside the gate.

The situation is a bit different in the nonfatal but disabling injury statistics. Of the over 10 million such injuries among the population last year, almost half (4,350,000) were workers, and almost half of these (2 million) occurred while he was at work. It is estimated that about 3 percent or 60,000 were due to occupational "disease," and the other 97 percent to occupational "injury," according to our previous definition.

With occupational deaths and injuries thus placed in some perspective, let us look at the kinds of occupations that are involved. Mining, quarrying, and construction had the highest death and injury rates last year, and trade and manufacturing had the lowest. Differences in death rates with a more than tenfold range from mining down to trade were more striking than the nonfatal injury rates which had little more than a twofold difference. One way of interpreting this is that a mining injury or a con-

struction injury is more likely to be fatal than a trade injury or a manufacturing injury.

What types of accidents are involved in these injuries and deaths? The New York State data show that about one-third of the accidents were of a "struck by" "struck against" nature. A quarter of them were due to slips and overexertion and one-fifth were due to falls. In one-ninth, the worker was caught in, by, or between. So far, we have accounted for 90 percent of the accidents, with the force of gravity being the ultimate responsible force for a good share of these. The remaining causes were inhalation, ingestion, and absorption, 3 percent; temperature extremes, 3 percent; continuous activity, 1 percent; and miscellaneous, 3 percent.

Where are these accidents occurring? If we inquire about the size of the organization, we find, for instance, that although half of all workers are found in businesses of 100 employees or fewer, this segment of the working population has more than two-thirds of the injuries. This is to say that injury frequency rates in small businesses are more than double those of large businesses. Why is this? One reason is that the small organization frequently doesn't have a strong health and safety program. It is not large enough, in most cases, to keep a full-time safety expert or medical staff busy, and the result, usually, is that it doesn't have any such people at all. It is a repeated source of surprise to me to find how large a company can get sometimes before it becomes enlightened about health and safety programs.

At this point it is tempting to neglect the toxic occupational problems. Just look at the data presented so far. If all problems of chemical hazard were completely solved there would be an almost imperceptible drop in the total work deaths and work injuries. So why bother? Well, I think there are at least five reasons:

1. The chemical injuries and deaths that occur are still that many too many. As long as there is a problem, there should be efforts to control the problem.

2. There is a relatively neglected segment of the working population which is exposed to greater than average toxic risks. In addition to having a poorer traumatic injury record, the small organization is more likely to have trouble with nontraumatic hazards such as chemical toxicity and radiation. In my own recent experience, I have seen cases of lead and mercury disease and overexposure in small plants. The toxicity of these elements has been known for 2,000 years, and few chemicals in use today have been studied as thoroughly. The current situations represent a lack of communication, not of fundamental information. Other old problems that are still popping up today are such things as benzene, carbon tetrachloride, carbon monoxide, arsenic, cyanide, silica, manganese, chromium, cadmium, vanadium, etc.

3. If it were not for the extensive hardware, procedural, and biological controls in operation today, the toxic problems would be many, many times worse. If present efforts were relaxed, the problem would increase.

4. New materials are emerging at a continuing rate. Whether they become safe and useful products or toxicologic nightmares depends on the alertness of those concerned with this sort of safety. Dr. Zapp will have more to say about this later, but I might briefly mention such things as the new "exotic" rocket fuels, the new pesticides, new hydraulic fluids, and components of the new plastics. It has been said that one good synthetic organic chemist can produce 100 new compounds for every one the toxicologist can evaluate, and there are 100 of these chemists for every toxicologist. There are some mitigating factors which make this disparity somewhat less than it may first appear, but the statement serves to draw attention to one problem in this field.

5. It is my job to point out the environmental problems today, not to solve them. However, one of the environmental problems is that we don't know some of the environmental problems. In the field of acute mechanical injury, there is rarely any doubt about the cause and effect relationship. If a man hits his finger with a hammer and the x-ray shows a broken bone, the establishment of cause is not difficult. Even the acute chemical injuries usually don't cause diagnostic trouble. However, when the cause is a protracted low-level exposure and the effect may be delayed and may be subtle, and particularly when it is a common condition seen in unexposed persons, too, diagnosis becomes difficult. Sometimes it is impossible.

Often the diagnosis cannot be made or even suspected in one individual. Then it is only when groups of workers are studied that the condition becomes evident. For example, almost anyone can get pneumonia, and such a person could be a manganese ore worker. It was not until someone observed that the incidence of pneumonia in a group of manganese ore workers was many times as high as the rest of the population that this disease was recognized as a toxic effect of the material. Similarly, the connection between chromates and lung cancer

was not established until the disease rates of chromate workers and an unexposed population were compared. This is called epidemiology, and we are going to need it more and more in the future as we look for more and more subtle effects of the working environment. Also, to support this epidemiology, we will need better and better data on the health of the workers over a long period of time. And this is difficult. Large companies and those with relatively stable populations can do this sort of health recording. The small organization and the one with a rapid turnover can't. It may be feasible for insurance carriers to do more of this. It would, of course, always be possible to do it by regulations.

In summary, we have discussed the following points:

1. Most accidental injuries and deaths occur off the job. Many workers are safer at work. Still, there are too many work injuries and deaths, and these are the concern of this Conference.

2. Most work accidents are of a mechanical nature. Injury from such agents as chemicals, radiation, temperature extremes, and electricity forms a relatively smaller segment of the total, but should not be forgotten. New hazards such as microwaves, the optical maser, and the plasma torch need continuing evaluation.

3. The most hazardous occupations are mining, quarrying, construction, and farming.

4. Small organizations are important because most workers are represented there and safety records are poorer there.

5. We should not neglect such nonmechanical areas as chemicals and radiation because new hazards are emerging rapidly in these fields, because the cause and effect relationship is usually more difficult to establish, and because undetected but nevertheless important amounts of disability may occur with these hazards.

6. There is currently a gap between the knowledge of the hazardous nature of a situation and its control in practice. If controls were to be improved just to the level permitted by our present knowledge, there would be a dramatic improvement in occupational injury and death rates. This is a matter of education. It is one of the aims of this Conference.

HOW INDUSTRY APPROACHES THE PROBLEM OF INSURING THAT ITS PROCESSES AND PRODUCTS ARE SAFE

Doctor John A. Zapp, Jr., Wilmington, Delaware

A discussion of how industry approaches the problem of insuring that its processes and products are safe must necessarily relate to a particular period of time for several reasons. For one thing, social thinking and the law concerning the responsibility of industry, of the individual, and of society as a whole, for the welfare of others has undergone a considerable change. For another, the technical knowhow required to make industrial operations safer for the worker, and the products of industry safer for the consumer, has grown steadily.

In this year 1964, it is possible to base our discussion on two goals. These are: (1) that conditions of employment should be such that no worker need inevitably sustain disease or injury as a result of his employment; and (2) that no product which is incapable of being used safely for its intended uses should be placed in the hands of the consumer.

Note that these goals do not guarantee safety for either the worker or the consumer. Anyone who works in a plant manufacturing dynamite can blow himself and the plant sky high if he is not careful, and the same is true of the man using the dynamite. But the large scale manufacture and use of dynamite also testify to the possibility of doing both of these things safely.

A. hundred, or even fifty, years ago, these goals would have been considered visionary and impractical. And while they are generally accepted today, there still are instances of injuries from processes and products which could be prevented.

As early as 1700 the Italian physician, Barnardino Ramazzini wrote a little book describing varieties of illness which were characteristic of a number of occupations. He states, for example, "Painters are also usually subject to various disorders, such as trembling of the joints, a cachexy, a blackness of the teeth, a discolored complexion, melancholy, and a loss of smell." Ramazzini considered it important that the physician always inquire about the trade of a patient he was called upon to treat, but the occurrence of these specific diseases of tradesmen seems to have been accepted as a matter of course.

Over a century later, the British pioneer in industrial medicine, Dr. C. T. Thackrah noted in 1831, that miners seldom attained the age of 40, that fork grinders who use a dry grindstone die at the age of 28 to 32, and that table knife grinders, on the other hand, who use wet stone survive to between 40 and 50. He further stated, "Most persons who reflect on the subject, will be inclined to admit that our employments are to a considerable degree injurious to health. . ." and he added, "Evils are suffered to exist, even when the means of correction are known and easily applied. Thoughtlessness or apathy is the only obstacle to success." This attitude, of suffering evils to exist, was characteristic of the time. To quote the Cambridge Modern History: "The Bolton cotton spinner of 1842 had no need to keep his children in health, or his house healthy; his wife could with absolute impunity let the babies die, the whole household was free, in fact to live practically as it chose, even if it infected and demoralized the neighborhood."

Fifty years ago in this country we were moving nearer to today's goals. Dr. W. G. Thompson, in his book "The Occupational Diseases" which appeared in 1914, stated, "It is quite true that many processes of manufacture will always involve risk to health, as many trades necessarily involve risk to limb and life. One cannot handle white lead without risk of disease, just as one cannot use dynamite without risk of injury. Yet, in each case, the workman has the right of warning against the hazard, the right of such protection as modern scientific knowledge affords, and should have the right of compensation when disabled as a result of the lack of such warning and protection." Yet Thompson had to say in the case of "boilermaker's deafness," "Unfortunately, there seems to be no remedy for this hazard. . . and, if a man must work inside a boiler or gun turret, he has to accept the consequences."

Thinking about a manufacturer's responsibility to the ultimate consumer of his products has also undergone an evolution. The old doctrine of "let the buyer beware" began to be eroded about 100 years ago when the purveyors of defective "inherently dangerous" articles, such as a defective gun or a mislabeled poison, were held liable for the use of "ordinary care." The trend of subsequent court decisions has been to steadily enlarge the responsibility of the manufacturer for injuries caused by his products, and the evolutionary process is still going on. A very readable summary of the current situation is found in an article by L. A. Coleman, which appeared in the November 1963 issue of the "Food Drug Cosmetic Law Journal."

When I first came with the Du Pont Company in 1945, my laboratory and office overlooked one of the old black powder mills on the banks of the Brandywine, dating from the early 19th century and long abandoned. The building had three very thick walls on the land side and a light wall facing the river. It was symbolic of the hazard of the black powder business. If anything went wrong, the contents and occupants of the building went out over the river. The hazard was minimized by all the techniques known at the time and by strictly limiting the size of the operation and the number of workmen in any one building. The hazard was sudden traumatic injury or death, and this was characteristic of much of industry at that time.

The kind of hazard involved with explosive or with moving machinery is usually quite apparent to the worker. He can literally see the danger. On the other hand, the kinds of hazard described by Ramazzini and his successors, which produce specific occupational diseases, are usually not so obvious and the workmen may be unaware that a hazard even exists. With the rise of the chemical industry, the latter category has become more important.

During the last quarter of the 19th century, the Du Pont Company began to get involved with two new explosives that recently invented by Alfred Nobel—dynamite and guncotton. In dynamite, the active ingredient was nitroglycerine, not only a powerful explosive, but also a powerful drug. In the beginning dynamite workers frequently suffered severe headaches, nausea, and sometimes collapse as a result of excessive exposure to nitroglycerine. With the realization that this new explosive could produce undesirable physiological effects, steps were taken to minimize the exposure.

There wasn't much chemical industry in the United States prior to World War I, and our dependence on the German chemical industry for such things as drugs, dyes, and other chemicals, stimulated efforts on the homefront. Du Pont, for example, decided to attempt the manufacture of aniline dyes. It was successful in the venture and still makes them.

That which is desired in a dye is color, but the color is achieved by reacting various aromatic nitro and amino "intermediate" compounds. These intermediates sometimes produced an unwanted bluish color in the workmen, that was caused by a reaction between the intermediates and hemoglobin which prevented the hemoglobin from combining with oxygen. Hence, arterial blood resembled venous

blood and imparted a dark bluish color to the complexion. This was a toxic effect which had nothing to do with the final colored product and which had not been anticipated.

The 1920's brought tetraethyl lead, a compound developed solely for the purpose of improving the performance of gasoline engines, but many of the chemists involved with the development apparently underestimated the hazard of working with a fat-soluble lead compound. Some deaths and a substantial number of cases of lead intoxication resulted.

In both of the above instances, toxicity was the unwanted and unanticipated attribute of chemicals developed to meet a particular technological need. Once the toxicity hazard was recognized, appropriate steps were taken to control the hazard. Dynamite, aniline dyes, and tetraethyl lead are still being manufactured, and with very good safety records.

With the rapid growth of the chemical industry following World War I, and particularly with the rise of synthetic chemistry, a great many new materials were made and found to fill some technological need. It seemed only logical that some, at least, of the new compositions of matter would have the unwanted attribute of toxicity. The question was how these could be recognized before the toxic effects were manifested in terms of human injury and disease.

The Haskell Laboratory for Toxicology and Industrial Medicine was the Du Pont Company's attempt to answer this question. It was opened in January 1935, as a laboratory of industrial toxicology whose function would be to study the toxic effects of new chemicals and processes on laboratory animals so that—from the information gained—the necessary precautions could be taken to manufacture the new chemicals safely. At about the same time, several other chemical companies established similar laboratories, and others have come into existence since then. Commercial laboratories and some universities offer similar services for those who do not have their own toxicological laboratories. Liability insurance companies are always ready to advise their clients on ways to reduce their risk. Many cities and states provide industrial hygiene services and will send experts into plants to survey the hazards and suggest improvements.

Basically, the industrial toxicological laboratory substitutes the exposure of laboratory animals for the exposure of man. It is meaningful to do this because the commonly used laboratory animals, mice, rats, rabbits, guinea pigs, and dogs, are constructed very much as we are. They all have hearts, lungs, liver, kidneys, etc. which perform the same functions as they do in man. There are obvious differences, of course, in overall size, shape, habits, diet, and life span, and these must, of course, be taken into account.

Suppose we set out to determine what amount of a chemical it takes just to kill a rat. We would find out first of all that individual rats differ in the amount required, but that the variation is by no means infinite. Rather, it resembles the kind of range in variation that we find in human heights and weights. We have short people and tall people, light people and heavy people, but there is a limit to the variation. We know from experience that men, like rats and other animals, also differ in their susceptibility to the toxic effects of chemicals and drugs. So man resembles the laboratory animals in this important aspect of toxicology. There is no such thing as a single minimum lethal dose that would apply to all men or to all rats, but we can determine a kind of average lethal dose of rats or other animals, and we should expect to find a kind of average lethal dose for man if there were any way of determining it experimentally.

Certainly, however, we would expect that it would take a much larger dose to kill a man than it would to kill a relatively tiny rat. The differences in size between the two, or any two, species can be compensated for by expressing the dose as a ratio to the body weight, e.g., milligrams of test substance per kilogram of body weight. On such a basis, the lethal dose of man, the rat, the dog, etc. move much closer together. We still have the problem, however, of possible species difference. Man may be relatively more or less susceptible than, say, the rat. By testing several species of animal, however, and assuming, in the absence of better knowledge, that man is at least as susceptible as the most sensitive species tested, we can at least approximate for working purposes what the average lethal dose for man might be. Such information is valuable for estimating what the chances for injury or death might be if a worker or consumer were to be inadvertently exposed to a given amount of the product.

We can obtain still more information from the kind of tests just described. All of the animals used in the test, whether they die or not, can be utilized. Survivors can be observed to determine whether recovery is rapid and complete or whether permanent damage has occurred. At given times the survivors can be sacrificed. These, along with those that died spontaneously, are examined by pathologists to determine what organs were affected and what kind of

damage was produced. This kind of information is essential for the physician if accidental exposure occurs.

The different routes by which chemicals get into the human body can also be duplicated with laboratory animals. These are inhalation of gases, vapors, mists and dusts; absorption through the skin; and ingestion. Furthermore, local effects on the skin and eyes can be observed.

So far, I have discussed the toxic effects of single exposures to chemicals. This is known as acute toxicity, and its effects are observed within minutes, hours, or a few days after the exposure. There is another kind of toxicity, however, which results from repeated exposures to daily doses, any one of which would produce no signs of toxicity whatever. This occurs when the toxic chemical accumulates in the body over a long period of time. It is called chronic toxicity, and is produced by some chemicals but not by others. The effects of chronic toxicity may not be manifested for months or years.

It is obviously important to determine whether a given chemical is capable of producing chronic toxic effects, and here again the laboratory animals are useful. Graded doses are administered daily to groups of animals for various periods of time and by the various routes of administration. Since rats, for example, live between 2 and 3 years, it is practical to administer the test chemical over their entire life span from childhood to senility and to observe the effects on growth, reproductive performance, behavior, and mortality. Biochemical studies can be carried out during life and pathological examination after death.

Two important laws of toxicity emerge from the animal experiments, both acute and chronic, and we believe that they apply also to man. They are: (1) the toxic effects of a chemical increase with increasing dose; and (2) a small but finite dose can be found which produces no detectable toxic effects whatever.

This second law is extremely important, for it tells us, in effect, that a poison is simply too much of any particular substance. For some materials, "too much" will be a very small absolute amount; for others, it may he a very large amount. It enables us to determine what kind of precautions need to be taken in manufacturing for its intended purpose. It is obvious, too, that toxicity studies on animals may guide us to the best and safest choice among competing candidate chemicals for a given use.

Given the necessary knowledge, manufacturers can and do manufacture and use extremely dangerous chemicals without injury to their employees. Consumers generally lack this expert knowledge, and therefore, must not only be given safer products, but must also be instructed on how to use them safely. The mechanism for reaching the consumer is ordinarily through that part of the product label which is commonly referred to as "precautionary information," although in some cases it may be through written instructions for use which accompany the product.

There has been a notable increase in recent years in both the quantity and quality of the precautionary information which reaches the consumer. Much of the type and form of the information on important classes of consumer products, such as pesticides and household products, is now prescribed by various State and Federal laws. Its goal is to call the attention of the consumer to those hazards which may not be immediately obvious—toxicity, flammability, explosibility, corrosiveness, radioactivity, etc.—and to set forth those conditions under which the product can be used safely.

In summary, I think we can say, in 1964, that industry has found reasonably effective ways of making sure that its processes and products are safe, providing that they are used safely. We no longer have to wait for adverse human experience to disclose the hidden hazards in processes and products because we can anticipate them through laboratory research. The goals which I set forth at the beginning of this talk are attainable, and although we can still say, as Thackrah said in 1931, "Thoughtlessness or apathy is the only obstacle to success," we no longer have to say with him: "Most persons who reflect on the subject will be inclined to admit that our employments are to a considerable degree injurious to health." And we can say with certainty that the products placed in the hands of the consumer today are immeasurably safer than they were over 50 years ago.

As we look to the future, however, we find that we are faced with a new problem which is the direct outgrowth of our rapidly expanding population. This is the contamination of our environment, of air, land, and water. More and more products are being made and used by more and more people. The result is an ever increasing outpouring of waste to reservoirs of air, land and water which are not increasing concomitantly.

The problem of environmental contamination is not only a problem for industry, but for all segments of the population. However, the chemical

industry, among others, recognizes that it has a responsibility in the field of environmental health. Perhaps this is best stated in the recommendations of a planning committee on environmental health which were made last year and approved by the Manufacturing Chemists' Association Board of Directors:

"The Manufacturing Chemists' Association, in view of the mounting environmental health problems of the nation, recognizes its responsibility for assisting in the reduction of these problems, and proposes to develop a more effective and better integrated program of information, education and action in this field.

"The chemical industry has been aware of, concerned about, and has worked to alleviate the problems of environmental health for many years. However, this awareness, concern, and effort has not always reached the entire industry either collectively or individually. Nor has it always gone beyond those problems which involve the industry directly.

"Population is increasing, available land area per person is declining, standards of living are advancing. All of these changes increase the demands man places on his environment and this load will continue to increase at an even faster rate. Early anticipation of problems and development of means of handling them before they become acute is more and more necessary. Such a comprehensive program requires the participation of each and every person and group in all society, including that segment which comprises the chemical industry."

As a result of the planning committee's recommendations, the Manufacturing Chemists' Association has set up a permanent Advisory Committee on Environmental Health. It is the goal of this committee to stimulate programs which will advance knowledge and increase competence to deal with industry's responsibilities within the total problem of environmental health. It is hoped that from this the chemical industry will be able to improve the appropriateness of its products by the best use of scientific knowledge, and by continuing to improve appropriateness as growing knowledge permits.

EDITORIAL DESK

LOCAL REPAIR OF HOSPITAL BEDS

The U.S. Naval Hospital, Portsmouth, New Hampshire, had 74 beds in good condition except that the head of the bed could not be raised or lowered because the threads in the adjustment mechanism had been stripped. Considerable effort was expended unsuccessfully in attempts to obtain replacement adjusting mechanisms.

During 1963, the problem was turned over to Mr. Wilfred L. Edwin, a maintenance man at the Hospital; he is now in the Portsmouth Shipyard Public Works Department and is regularly assigned to the Hospital.

Mr. Edwin solved the problem by cutting the 2-inch stripped gear section out of the adjusting mechanism as illustrated below in Exhibit "A". Exhibits "B" and "C" illustrates the dimensions of the brass stock and the cutting and threading dimensions required to make a replacement busing section. Exhibit "D" illustrates and describes the finished new section, plus the two threading taps required; if not on hand locally. Exhibit "E" shows the completed bushing section ready for installation. Exhibit "F" illustrates the bushing section in place and being brazed.

Additional description of the procedure follows:

1. The removal of the "2" section of the operating tube, shown in Exhibit "A", was accomplished with a hacksaw.

2. The "blank" depicted in Exhibit "B" was made by this Hospital's automechanic using a medium size shop lathe.

3. The threading operation depicted in Exhibit "C" is done by hand with the blank held in a pipe vise. This operation takes approximately 15-20 minutes for each bushing.

4. Exhibit "D" shows a small hole made into the completed bushing to permit a periodic lubrication with graphite which was *not* possible in the original assembly.

5. In addition to providing twice the thread

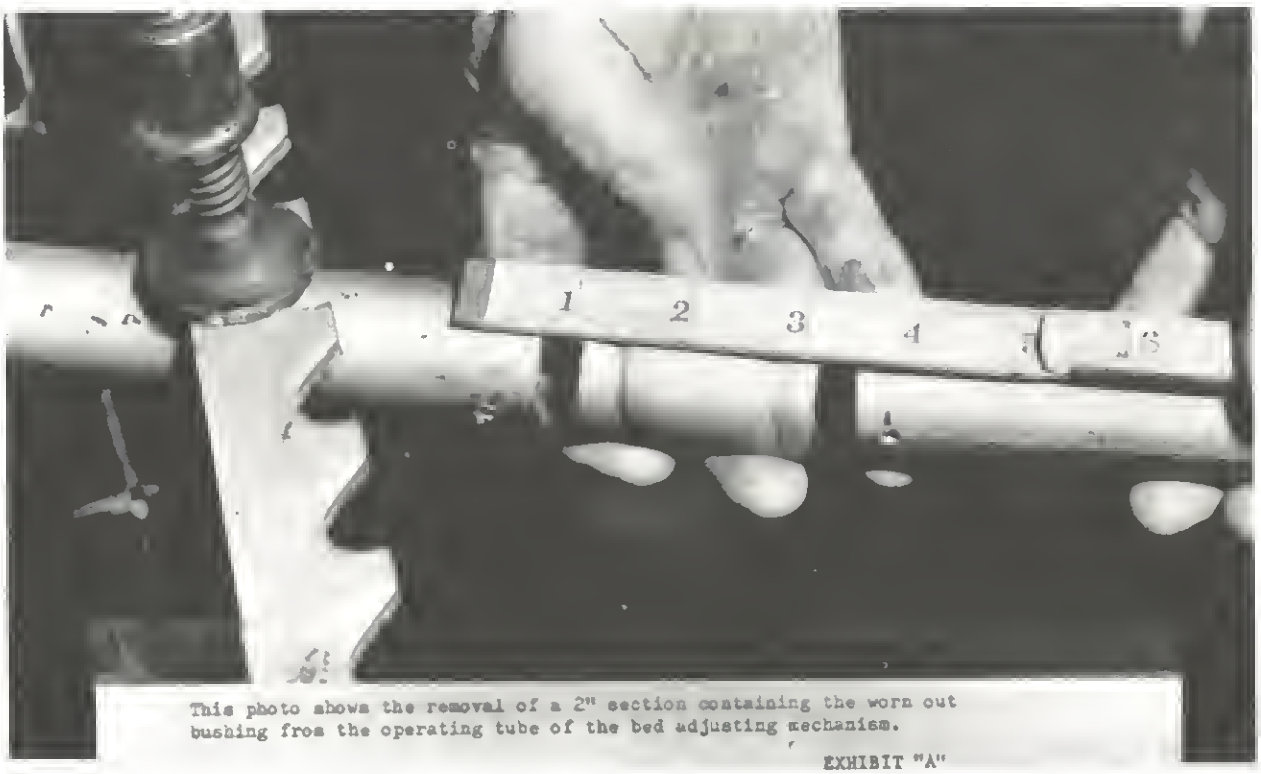
length, the milled ends of the new busing (see Exhibit "E") provide increased stability for the new bushing in the operating tube. Before installing the new bushing, the insides of both seetions of the tube are reamed slightly with a rotary file to permit the snug insertion of the milled ends. This inereased stability and longer thread length provided better alignment and smoother aetion of the operating screw.

6. Exhibit "F" shows the brazing operation in which the silver solder is introduced through holes previously drilled in the operating tube. These holes (4 on eaeh end of the severed tube) are dirceily over the middle of the inserted milled portions of the new bushing and thereby insures adequate bonding of the new busing to the inside wall of the operating tube.

7. Finally, the use of the thread taps (both rougher and finisher) is neeessary, not only to make the bushings, but also in the final step of the procedure. The brazing operation leaves a certain amount of slag and excess solder in threads; and the taps must then *again be run through before inserting the operating screw* and reassembling the adjusting mechanism.

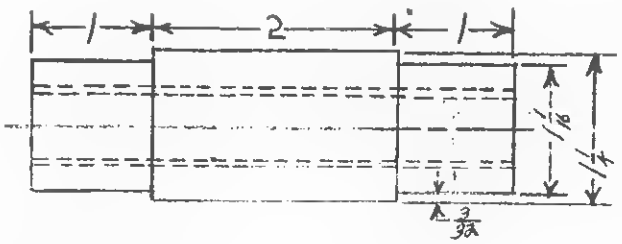
Excluding the eost of the two threading taps, the eost of labor and materials was estimated at $7.50 per bed. Several of the repaired beds have been in use sinee Novembcr 1964 and are continuing to function properly. Mr. Edwin received a local beneficial suggestion award and his suggestion has been forwarded via higher authority for additional consideration.

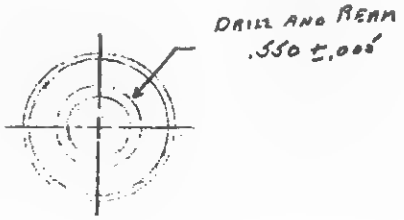
This idea is disseminated for use by other activities, if applicable.—Code 4, BUMED.



This photo shows the removal of a 2" section containing the worn out bushing from the operating tube of the bed adjusting mechanism.

EXHIBIT "A"

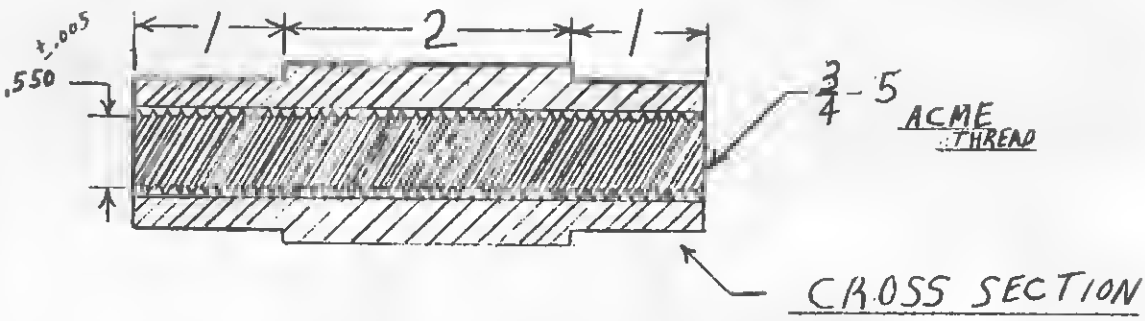




NOTE:
DIMENSIONS ON LENGTH AND SHOULDERS MAY VARY. 1/8" PLUS OR MINUS

MATERIAL: HALF HARD NAVY BRASS	24 JUNE 1963
AVAILABLE AS STANDARD STOCK ITEM	SCALE 1" = 1"

EXHIBIT "B"

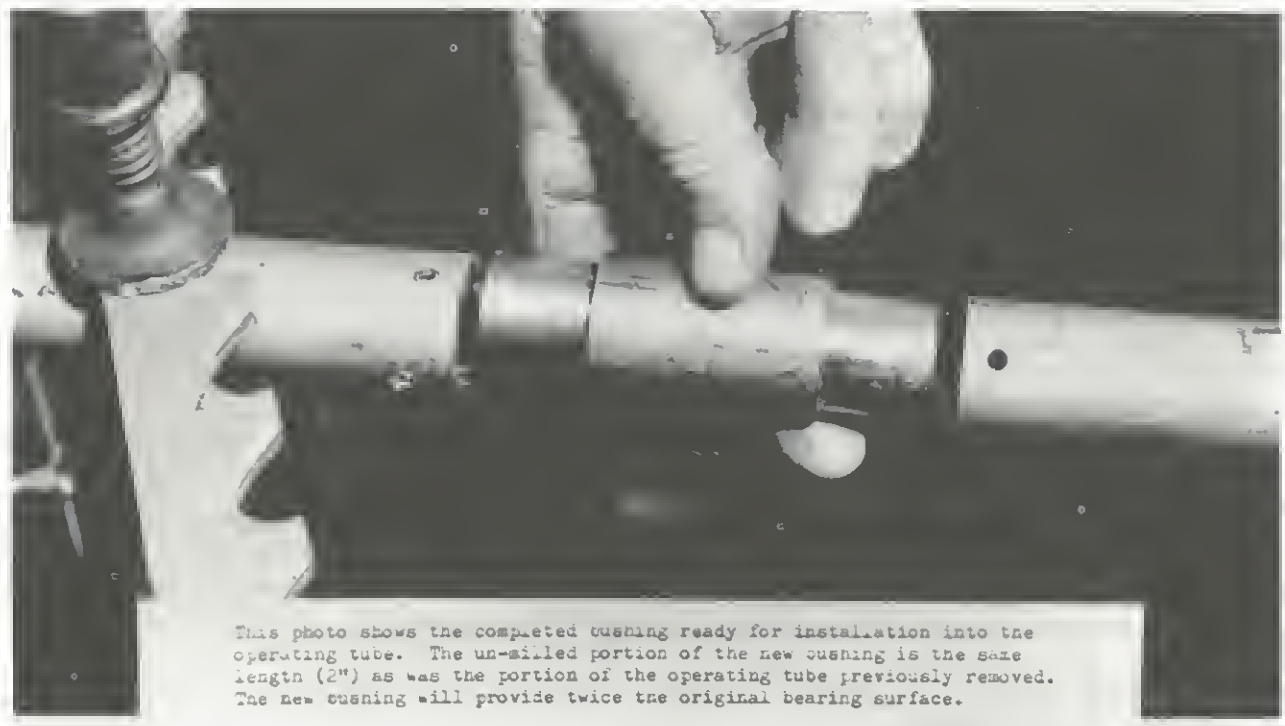


MATERIAL HALF HARD NAVY BRASS	24 JUNE 1963
AVAILABLE AS STANDARD STOCK ITEM	SCALE 1" = 1"

EXHIBIT "C"

This photo shows the completed new ⅜" threaded bushing flanked by the two thread taps used in it's manufacture. The thread taps are technically described as: Set of two (2) ⅜"-5 Acme high speed ground thread taps, consisting of 1 rougher and 1 finisher .4" O/All" thread length and ⅜" long plain pilot for tapping 5" through medium hard brass. Hole size is .550. Approximate cost $[illegible].00

EXHIBIT "D"



This photo shows the completed bushing ready for installation into the operating tube. The un-milled portion of the new bushing is the same length (2") as was the portion of the operating tube previously removed. The new bushing will provide twice the original bearing surface.

EXHIBIT "E"

This photo shows brazing the new bushing into the operating tube. Materials used: low temperature brazing flux and #4 silver solder (.110 wire). In the final step, the thread taps (rougher and finisher) are again run through the new-threaded bushing to clean out and slag or excess solder resulting from the brazing operation, and the adjuster mechanism re-assembled.

EXHIBIT "F"

COMMENDATION FOR ACHIEVEMENT

The Secretary of the Navy takes pleasure in commending Nelson E. Hall, Hospital Corpsman First Class, U.S.N., for outstanding achievement in the superior performance of his duties as set forth in the following CITATION:

During the period 12 December 1963 to 14 February 1965 while serving as petty officer in charge of the Medical Department in USS DAMATO (DD–871), HALL was responsible for all of the details of assembly of supplies and materials, inspection of spaces and facilities, organization of the Medical Department, and medical training of the crew in DAMATO upon completion of FRAM I overhaul. Attesting to the efficiency and thoroughness of his work were consistent superior evaluations in the medical area of inspections aboard DAMATO culminating in an evaluation of outstanding with a grade of 97.5 by Commander Cruiser-Destroyer Force, U.S. Atlantic Fleet, on a surprise medical inspection on 11 February 1965. By his outstanding technical skill, leadership, and inspiring devotion to duty, Hall contributed materially to the readiness of the DAMATO and to the morale of seniors and juniors alike, thereby upholding the highest traditions of the United States Naval Service.

S/Paul H. Nitze

MEDICAL ASPECTS OF ADVANCED WARFARE

NOTE: Change in dates and location of course.

CLASS	INCLUSIVE DATES
OZR 9300–4	15–19 November 1965

DEADLINE DATE TO APPLY
1 October 1965

The above course will be conducted by the U.S. Air Force, at the Medical Service School, Gunter Air Force Base, Alabama.

Secret Security Clearance is required on all candidates for attendance, and selections will be on a "need-to-know" priority basis.

Requests should be forwarded in accordance with BUMED INSTRUCTION 1520.8A and comply with the deadline date as indicated above. All requests must indicate that a security clearance of SECRET has been granted to the officer requesting attendance, and an explanation in regard to their "need-to-know."

This change supersedes the former announcement in the U.S. Navy Medical News Letter 46(1) of 9 July 1965.—Training Branch, BUMED.

FIRST TEAM SELECTED FOR NAVY'S SEALAB II

Washington (AFPS)—The Navy has named a 10-man team to make the first 15-day run in Project SEALAB II, the longest man-in-the-sea experiment yet attempted.

SEALAB II, planned to last at least 30 days, will be conducted at a depth of approximately 210 feet off the coast of La Jolla, Calif.

At the end of the first 15-day run, eight of the men will be replaced. Two will continue for the full time of the experiment. The men were selected from 35 who have been training since May at the U.S. Naval Mine Defense Laboratory, Panama City, Fla.

Captain of the first team to submerge is Commander M. Scott Carpenter, on loan from the National Aeronautics and Space Administration.

NORMAN A. WELCH, M.D., MEMORIAL AWARD

Norman A. Welch, M.D., active in Blue Shield at both the local and national levels for many years and president of the American Medical Association when he died on September 3, 1964, was one of the leading figures in American medicine.

Dr. Welch served the cause of medicine and Blue Shield for many years. He was president of Massachusetts Medical Service from 1950 until he became president-elect of the AMA in 1963. He was president and chairman of the board of the Blue Shield Commission—the forerunner of the National Association of Blue Shield Plans—from 1955 until 1958. Elected to the AMA's House of Delegates in 1951, he served as speaker of that body from 1959 to 1963.

Dr. Welch received his M.D. degree from Tufts College Medical School in 1926. He later taught at Tufts and the Boston University School of Medicine. He was also a consultant to various state institutions and hospitals in the Boston area.

The 1965 Norman A. Welch, MD., Memorial Award will be presented by the National Association of Blue Shield Plans to the author of the most scholarly and meritorious contribution to the literature of medical economics. The work can be an article or a series of articles, a book, or a speech published or presented between July 1, 1964, and June 30, 1965. The sole criterion in judging will be the merit of the work.

A medallion of solid gold emblazoned with a bust of Dr. Welch will be awarded to the author. In addition, $1,000 will be contributed in the author's name to the Norman A. Welch Memorial Fund of the American Medical Association Education and Research Foundation. This fund is used to guarantee loans to medical students.

The award winner will be selected by a three-man committee composed of representatives of the American Medical Writers' Association, American Medical Association, and the board of Directors of the National Association of Blue Shield Plans. The literature to be judged will be compiled by the library of the National Association of Blue Shield Plans. Authors wishing to submit entries may do so by sending three copies of their work to: Norman A. Welch, M.D., Memorial Award, National Association of Blue Shield Plans, 425 N. Michigan, Chicago, Illinois 60611. Deadline for submitting entries is September 15, 1965.

The announcement of the winner and the presentation of the award will be made at the 1965 Annual Program Conference of the National Association of Blue Shield Plans in Chicago on October 25, 1965.

The Norman A. Welch, M.D., Memorial Award will be presented on an annual basis.

MAURICE C. SHEPARD, PH.D., HONORED

Maurice C. Shepard, Ph.D., was honored by election to the New York Academy of Sciences on 24 June 1965. This honor was extended in recognition of Dr. Shepard's sustained interest in creditable contributions toward the advancement of science which was deemed to unreservedly qualify him for affiliation with the Academy. Dr. Shepard is Chief of the Bacteriology Division of this laboratory, and resides with his family at 1008 River Street, Jacksonville, North Carolina.

The New York Academy of Sciences has as its purpose: To advance scientific research and discovery, provide a forum for presentation and discussion of scientific problems, publish and distribute results of research, and interpret them for promotion of common welfare. The Academy is comprised of many pre-eminent and internationally-known scientists.

Dr. Shepard recently authored an article entitled, "The Role of Mycoplasma (Pleuropneumonia-like Organisms) in Human Disease."

DEPARTMENT OF THE NAVY

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NATIONAL NAVAL MEDICAL CENTER
BETHESDA, MARYLAND 20014